Remarks

Non-elected claims 2-11 have been canceled without prejudice to or disclaimer of the underlying subject matter. Claim 1 has been amended to reflect the elected SEQ ID NO: 5. Claims 12 through 19 have been added. Support for the foregoing claim amendments and new claims may be found throughout the specification, for example at page 19, line 2 through page 20, line 7; at page 37, line 16 through page 39, line 23, in Table A, in the sequence listing, and in the original claims. No new matter enters by way of these amendments. Upon entry of the foregoing amendments, claims 1 and 12-19 are pending in the application.

The specification has been amended to explicitly reference the Sequence Listing on computer readable form in the present application. In addition, the Examiner describes pages 14, 16, and 48 of the disclosure as containing embedded hyperlinks and/or other forms of browser executable code. Applicants respectfully disagree; however in order to facilitate prosecution, the specification has been amended to remove the alleged embedded hyperlinks and/or other forms of browser-executable code. The URL addresses themselves contained throughout the specification do not constitute browser-executable code in the absence of embedded hyperlinks and/or other forms of browser-executable code. The specification as amended does not contravene stated PTO policy of prohibiting live web links to other web pages, which might be commercial. (MPEP, § 608.01). No new matter enters by these amendments.

As requested by the Examiner, the specification has been amended to correct typographical errors in the claim for priority. No new matter enters by this amendment.

1. Election/Restriction Requirement

Applicants acknowledge the finality of the restriction requirement but maintain their traversal. To facilitate prosecution, however, Applicants have removed the non-elected claims 3-11 from the application. Applicants respectfully point out that the application as originally filed contained claims 1-11. In response to the Office Action mailed October 7, 2002, Applicants provisionally elected Group I, claims 1 and 2. The

current Office Action incorrectly identifies claims 1-7 as pending in the application and claims 3-7 as withdrawn from consideration. Office Action at pages 1-2.

Applicants further acknowledge the finality of the election requirement to a single nucleotide sequence, but maintain their traversal. Applicants submit that election of a single nucleotide sequence is improper, and Applicants believe no serious burden would result by the search and examination of at least ten nucleotide sequences. The election of a single nucleic acid sequence contravenes the USPTO policy as set forth in the Manual of Patent Examining Procedure stating that "to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided ... to permit a reasonable number of such nucleotide sequences to be claimed in a single application." (MPEP, 8th ed., August 2001, Section 803.04). The MPEP further provides that "[i]t has been determined that normally ten sequences constitute a reasonable number for examination purposes." (emphasis added) *Id.* While the Examiner requires that a single nucleotide sequence be selected, no reason has been provided for this deviation from articulated Patent Office policy.

Although Applicants disagree with the election requirement of a single nucleotide sequence, to facilitate prosecution the claims have been amended to reflect the elected SEQ ID NO: 5.

2. Rejection of Claims 1-2 Under 35 U.S.C. § 112, First Paragraph, Written Description

The Examiner has rejected claims 1-2 under 35 U.S.C. § 112, first paragraph, for allegedly lacking an adequate written description. Office Action at pages 3-5. Applicants respectfully traverse this rejection. As Applicants have cancelled claim 2, the following arguments are addressed to pending amended claim 1.

Although the Examiner acknowledges that "[c]laims limited to isolated polynucleotides consisting of SEQ ID NO: 5 would meet the written description provision of 35 U.S.C. 112, first paragraph", claim 1 allegedly fails to meet the written description requirement because "[t]he specification provides insufficient written

description to support the genus encompassed by the claims." Office Action at page 4. Applicants respectfully disagree with this contention.

An adequate written description of a genus of nucleic acids, as recited in claim 1 may be achieved by either "a recitation of a representative number of [nucleic acid molecules], defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus." *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69 (Fed. Cir. 1997). The feature relied upon to describe the claimed genus must be capable of distinguishing members of the claimed genus from non-members. *Id.*

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989). A related, and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985), *quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981). Thus, in order for Applicants to describe each and every molecule encompassed by the claims, it is not required that every aspect of those nucleic acid molecules (*e.g.*, an open reading frame) be disclosed. *In re Alton,* 76 F.3d 1168, 1175 (Fed. Cir. 1996) (if a person of ordinary skill in the art would, after reading the specification, understood that the inventor had possession of the claimed invention at the time of filing, even if not every nuance, then the written description has been met).

The Examiner further contends that "[o]ne of skill in the art would not be able to determine what fragments, and mutants or alleles would fall within the scope of the claims". Office Action at page 4. According to the Examiner, proper written description support for a claim directed to a nucleic acid sequence requires nothing less than the actual disclosure of every sequence encompassed by that claim. In support of this proposition, the Examiner relies on *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). Applicants respectfully disagree. In *Eli Lilly* the court found that claims to a vertebrate cDNA coding insulin were inadequately described. However, the present case is clearly different. Specifically, the present claims "distinguish the claimed genus from others" and define "structural features commonly possessed by members of the genus that distinguishes them from others," unlike the claims at issue in *Eli Lilly*. *Id.* at 1568-69 ("a cDNA is not defined or described by the mere name 'cDNA'...but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA.").

In particular, Applicants have provided a detailed chemical structure, *i.e.*, the nucleic acid sequence of SEQ ID NO: 5. Moreover, nucleic acid molecules falling within the scope of claim 1 are readily identifiable – they comprise a nucleic acid molecule having the nucleic acid sequence of SEQ ID NO: 5. The fact that the nucleic acid molecules may comprise additional sequences or variations is beside the point. Such modifications are readily envisioned by one of ordinary skill in the art and disclosed throughout the present specification. Thus, there is no deficiency in the written description support for claim 1. Therefore, claim 1 satisfies the written description requirement of 35 U.S.C. § 112, first paragraph. Reconsideration and withdrawal of this rejection are respectfully requested.

3. Rejection of Claims 1-2 Under 35 U.S.C. §112, First Paragraph, Enablement

Claims 1-2 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled by the specification under an analysis of the factors presented in *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1998). Office Action at pages 6-

8. As Applicants have cancelled claim 2, the following arguments are addressed to pending amended claim 1.

The Examiner rejects claims 1-2 as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Office Action at page 6. While the Examiner concedes that "[t]he specification provides guidance for making the particular short EST sequences which were elected", the Examiner argues that there would allegedly be "an unpredictable amount of experimentation required to practice the claimed invention." *Id.* Applicants respectfully disagree and assert that a reasonable analysis of the *In re Wands* criteria leads to the conclusion that the claimed invention would not require undue experimentation to make and use the claimed nucleic acid molecules, alone and in combination with other nucleic acid molecules in the disclosed utilities.

It is well established patent jurisprudence that Applicants needs not teach "conventional and well-known genetic engineering techniques" (*see, for example, Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000)), which would include the use of the claimed sequence with other nucleic acid sequences, Applicants submit the Examiner has not met the required burden. Furthermore, Applicants submit that an analysis of the criteria presented by *In re Wands* supports Applicants' position that no undue experimentation would be required to make and use the claimed invention. *Id.*

The first *Wands* criterion is the quantity of experimentation necessary. As mentioned above, the "make-and-test" "quantum" of experimentation is reduced by the extensive knowledge, for example of conservative nucleotide substitutions and of hybridization parameters, to which a person of ordinary skill in the art has access. *See*, for example, the hybridization parameters set forth in Sambrook *et al.* (eds.), *Molecular Cloning: A Laboratory Manual*, 2d ed., pp. 9.47-11.61, Cold Spring Harbor Laboratory Press, Plainview, New York (1989) and Haymes *et al.*, *Nucleic Acid Hybridization, A Practical Approach*, IRL Press, Washington, D.C. (1985). Performing routine and well-

known steps, such as sequence alignment protocols, molecular weight determination, and antibody hybridization assays, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976). Thus, the addition of nucleotides to the recited sequence, nucleic acid molecules that hybridize to the claimed nucleic acid molecules, and knowledge of variations in the claimed nucleic acid molecules that encode a protein having one or more conservative amino acid substitutions is rendered predictable to one of ordinary skill in the art. Accordingly, it is well-within the ability of one skilled in the art to make or identify the claimed isolated nucleic acid molecules.

The second *Wands* criterion relates to the amount of direction or guidance given. The specification provides guidance, for example, on hybridization parameters in the context of the disclosed utilities and guidance on conservative substitutions in amino acid sequences. Such direction or guidance includes: illustrative hybridization conditions (specification at page 38, line 14 through page 39, line 8); references setting forth methodology that includes the hybridization of nucleic acid molecules to detect polymorphisms (specification at page 45, line 1 through page 47, line 6); references setting forth methodology that includes the hybridization of nucleic acid molecules for *in situ* hybridization (specification at page 73, line 1 through page 74, line 18); and references setting forth conservative substitutions in amino acid sequences (specification at page 42, lines 3 through page 43, line 21 and Table A).

The third *Wands* criterion relates to the presence or absence of working examples. The specification provides, for example, isolation of the claimed nucleic acid molecules, evidence of sequence identity, and discusses the use of the claimed SEQ ID NO: 5 in expression systems and the use of the claimed SEQ ID NO: 5 to isolate additional sequences within a genome. *See, e.g.,* specification at page 208, line 10 (Table A) and page 206, line 5 though page 207, line 6 (Example 3); page 124, line 3 through page 127, line 15; page 169, line 9 through page 170, line 2 (Example 1), and the sequence listing. Based on such disclosure, one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with the claims.

The fourth criterion focuses on the nature of the invention. The present invention relates to nucleic acid molecules, their complements, and nucleic acid molecules that hybridize to the claimed nucleic acid molecules, and the specification further describes amino acid sequences derived therefrom, antibodies, constructs and methods related thereto. *See, e.g.,* specification at page 40, line 12 through page 43, line 22 (describing polypeptide molecules and homologues); page 83, line 16 through page 92, line 8 (describing use of the claimed nucleic acid molecules in methods of transforming plants); and page 92, line 9 through page 100, line 18 (construction of expression vectors from the nucleic acid molecules of the present invention).

The fifth and sixth criteria focus on the state of the art and the relative skill in the art. Methods needed to practice the invention are known in the art as well as procedures to carry out the hybridization steps. *See*, for example, Sambrook *et al., Molecular Cloning: A Laboratory Manual,* Cold Spring Harbor (1989), Mailga *et al., Methods in Plant Molecular Biology,* Cold Spring Harbor (1995) and Birren *et al., Genome Analysis: Analyzing DNA,* 1, Cold Spring Harbor (1997) and Haymes *et al., Nucleic Acid Hybridization, A Practical Approach*, IRL Press, Washington, DC (1985). These references are available to guide use of the claimed nucleic acid molecules. It is clear from these resources, particularly the guidance given on how to carry out the hybridization step, that a person of ordinary skill in the art would be able to use the claimed nucleic acid molecules for the disclosed utilities. Practitioners in this art have available to them considerable knowledge on the conditions and approaches that can be utilized for such a step. As the Examiner has acknowledged, "the skill of those in the art of molecular biology is high." Office Action at page 7.

Furthermore, the Examiner's reliance on Moffatt (U.S. Pat. No. 5,770,718) and Moffatt *et al., Gene 143:*211-216 (1994), to establish lack of enablement of the claimed nucleic acid molecules is misplaced. Although the Examiner contends the U.S. Patent No. 5,770,718 supports the assertion that the claimed invention is not enabled because "differing known genes are *lacking in sequence similarity*, and that previous hybridization experiments to identify APRT encoding sequences had been unsuccessful" (Office Action at page 7) (emphasis in original), what the patent actually says is that

attempts to isolate the apt cDNA in *Arabidopsis* via cross-hybridization with previously isolated apt sequences (*e.g.*, sequences isolated for mouse, hamster and human) were unsuccessful. *See* Col. 2, ll. 50-65, col. 3, l. 52 – col. 4, l. 4. The state of the art must be evaluated based on the filing date of the present application. *See* MPEP § 2164.05(a). Instead, the Examiner's enablement evaluation ignores the sequence disclosed by the Applicants and, as such, it is not proper for the Examiner to conclude based solely on this reference that Applicants' invention would not have been enabled as of its filing date. The Examiner also contends in the Office Action at page 9 that the "sequence of Moffatt has significant homologies to the elected polynucleotide sequence". Thus, contrary to the examiner's assertion, one skilled in the art could use the nucleic acid molecules of the claimed invention for the disclosed utilities.

The seventh criterion considers the predictability of the art. The Examiner has presented no evidence why one of ordinary skill in the art would not, for example, be able to predict conservative amino acid residue substitutions, identify portions of ARPT encoded by the claimed nucleic acid molecules, use the nucleic acid molecules of the present invention in conjunction with promoter sequences known in the art (*see* specification at page 107, lines 11-24), or use the nucleic acid molecules of the present invention in conjunction with other molecules for the disclosed utilities. Thus, as discussed above, the specification provides sufficient guidance to one of skill in the art to decipher the information necessary to make and use the claimed nucleic acid molecules.

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). Here, enablement is satisfied because the art worker is guided by the disclosure to look, for example, to known hybridization parameters and sequence identity in making that determination. As previously stated, performing routine and well-known steps, such as sequence alignment protocols, molecular weight determination, and antibody hybridization assays, cannot create undue experimentation even if it is

laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

The Examiner has presented no evidence supporting the allegation that one of ordinary skill in the art would not be able to make or use the claimed nucleic acid molecules and constructs in light of the Applicants' disclosure. Furthermore, the analysis of the *Wands* factors, discussed *supra*, conclusively establishes that one of ordinary skill in the art would be able to make and use the claimed invention based on the disclosure in the specification. Accordingly, for at least these reasons, the enablement rejection of claim 1 under 35 USC § 112, first paragraph, is improper. Reconsideration and withdrawal are respectfully requested.

4. Rejection of Claims 1 and 2 Under 35 U.S.C. § 112, Second Paragraph

Claims 1-2 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting non-elected embodiments of the invention. Office Action at page 8.

Applicants have amended claim 1 and canceled claim 2 to reflect the elected SEQ ID NO: 5. As such, the rejections under 35 U.S.C. § 112, second paragraph, have been rendered moot by these foregoing claim amendments. Reconsideration and withdrawal of this rejection are respectfully requested.

5. Rejection of Claims 1-2 Under 35 U.S.C. §102

Claims 1-2 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Moffatt (U.S. Patent No. 5,770,718). Applicants respectfully traverse this rejection.

"It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Further, "an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device." *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q 619 (Fed. Cir. 1985).

In the present application, the presently amended claim 1 is directed to a substantially purified nucleic acid molecule that encodes a maize or a soybean adenine phosphoribosyl transferase or fragment thereof comprising the nucleic acid sequence of SEQ ID NO: 5. The reference cited by the Examiner does not disclose SEQ ID NO: 5. The Office Action alleges that "[t]he sequence of Moffatt has significant homologies to the elected polynucleotide sequence, with stretches of complete identity." Office Action at page 9. However, the Examiner has not identified the extent of homology disclosed in this reference nor has the Examiner shown that SEQ ID NO: 5 is disclosed by Moffatt.

As such, the presently amended claims are not anticipated by the Moffatt reference cited by the Examiner. Absent a teaching of each and every element of the claim, the reference cited by the Examiner under §102(e) does not anticipate the presently amended claim 1.

Accordingly, for at least the foregoing reasons, the rejection of claims 1-2 under 35 U.S.C. § 102(e) is improper. Furthermore, the amendment of claim 1 has rendered moot the rejections under §102. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-2 have also been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Moffatt *et al.* (Moffatt *et al.* 1994 Gene vol. 143 pages 211-216).

"It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Further, "an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device." *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q 619 (Fed. Cir. 1985).

In the present application, the presently amended claim 1 is directed to a substantially purified nucleic acid molecule that encodes a maize or a soybean adenine phosphoribosyl transferase or fragment thereof wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO: 5. The Office Action alleges that "[t]he sequence of Moffatt et al. has significant homologies to the elected polynucleotide sequence, with stretches of complete identity." Office Action at pages 9-10. However,

the Examiner has not identified the extent of homology disclosed in this reference nor has the Examiner shown that SEQ ID NO: 5 is disclosed by this reference. Absent a teaching of each and every element of the claim, the reference cited by the Examiner under §102(b) does not anticipate presently amended claim 1.

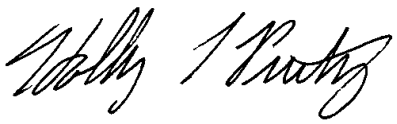
Accordingly, for at least the foregoing reasons, the rejection of claims 1-2 under 35 U.S.C. § 102(b) is improper. Furthermore, the amendment of claim 1 has rendered moot the rejections under §102. Reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance, and notice of such is respectfully requested. The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe that any fees in addition to those provided for in the accompanying documents, are due at this time. However, if any fees under 37 C.F.R. §§ 1.16 or 1.17 are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Deposit Account No. 50-2387, referencing docket number 16517.256.

Respectfully submitted,



Holly Logue Prutz (Reg. No. 47,755)
David R. Marsh (Reg. No. 41,408)

Date: March 19, 2003

ARNOLD & PORTER
555 Twelfth Street, N.W.
Washington, D.C. 20004-1206
(202) 942-5000 telephone
(202) 942-5999 facsimile

Marked-up Version of Amended Specification

At page 1, line 4 through page 2, line 5:

This application claims priority under 35 U.S.C. § 120 as a continuation-in-part of pending application No. 09/199,129 filed November 24, 1998; as a continuation-in-part of application No. 09/210,297 filed December 08, 1998 (now abandoned); and as a continuation of application No. 09/227,586 filed January 08, 1999 (now abandoned); and claims priority under 35 U.S.C. §119(e)[and/or 35 U.S.C § 120 of] to U.S. Provisional A[a]pplications No. 60/067,000 filed November 24, 1997; No. 60/069,472 filed December 9, 1997; No. 60/071,064 filed January 9, 1998; No. 60/074,201 filed February 10, 1998; No. 60/074,281 filed February 10, 1998; No. 60/074,567 filed February 12, 1998; No. 60/074,565 filed February 12, 1998; No. 60/075,462 filed February 19, 1998; No. 60/075,461 filed February 19, 1998; No. 60/075,464 filed February 19, 1998; No. 60/075,460 filed February 19, 1998; No. 60/075,463 filed February 19, 1998; No. 60/077,231 filed March 9, 1998; No. 60/077,229 filed March 9, 1998; No. 60/077,230 filed March 9, 1998; No. 60/078,368 filed March 18, 1998; No. 60/080,844 filed April 7, 1998; No. 60/083,067 filed April 27, 1998; No. 60/083,387 filed April 29, 1998; No. 60/083,388 filed April 29, 1998; No. 60/085,224 filed May 13, 1998; No. 60/085,223 filed May 13, 1998; No. 60/085,222 filed May 13, 1998; No. 60/086,186 filed May 21, 1998; No. 60/086,187 filed May 21, 1998; No. 60/086,185 filed May 21, 1998; No. 60/086,184 filed May 21, 1998; No. 60/086,188 filed May 21, 1998; No. 60/089,524 filed June 16, 1998; No. 60/089,810 filed June 18, 1998; No. 60/089,814 filed June 18, 1998; No. 60/090,170 filed June 22, 1998; No. 60/092,036 filed July 8, 1998; No. 60/099,670 filed September 9, 1998; No. 60/099,697 filed September 9, 1998; No. 60/100,674 filed September 16, 1998; No. 60/101,132 filed September 21, 1998; No. 60/101,130 filed September 21, 1998; No. 60/101,508 filed September 22, 1998; No. 60/101344 filed September 22, 1998; No. 60/101347 filed September 22, 1998; No. 60/101,343 filed September 22, 1998; No. 60/104,126 filed October 13, 1998; No. 60/104,127 filed October 13, 1998; No. 60/104,124 filed October 13, 1998; No. 60/104,121 filed October 13, 1998; and No. 60/111,981 filed December 11, 1998[, No. 09/199,129 filed November

24, 1998; No. 09/210,297 filed December 08, 1998; and No. 09/227,586 filed January 08, 1999] the disclosures of which applications are herein incorporated by reference in their entirety.

At page 14, lines 6 to 14:

Similarity analysis includes database search and alignment. Examples of public databases include the DNA Database of Japan (DDBJ) (www-[.]ddbj.nig.ac.jp/); Genebank (www-[.]ncbi.nlm.nih.gov/Web/Search/Index.html[lm]); and the European Molecular Biology Laboratory Nucleic Acid Sequence Database (EMBL) (www-[.]ebi.ac.uk/ebi_docs/embl_ db/embl_db.html). Other appropriate databases include dbEST (www-[.]ncbi.nlm.nih.gov/ dbEST/index.html), SwissProt (www-[.]ebi.ac.uk/ebi_docs/swisprot_db/swisshome.html), PIR (www-nbrt.georgetown.edu/pir/) and The Institute for Genome Research (www-[.]tigr. org/tdb/tdb.html).

At page 16, lines 5 to 21:

Homologues in other organisms are available that can be used for comparative sequence analysis. Multiple alignments are performed to study similarities and differences in a group of related sequences. CLUSTAL W is a multiple sequence alignment package available that performs progressive multiple sequence alignments based on the method of Feng and Doolittle, *J. Mol. Evol.* 25: 351-360 (1987), the entirety of which is herein incorporated by reference. Each pair of sequences is aligned and the distance between each pair is calculated; from this distance matrix, a guide tree is calculated, and all of the sequences are progressively aligned based on this tree. A feature of the program is its sensitivity to the effect of gaps on the alignment; gap penalties are varied to encourage the insertion of gaps in probable loop regions instead of in the middle of structured regions. Users can specify gap penalties, choose between a number of scoring matricies, or supply their own scoring matrix for both the pairwise alignments and the multiple alignments. CLUSTAL W for UNIX and VMS systems is available by ftp at: [ftp.ebi.ac.uk] ebi.ac.uk. Another program is MACAW (Schuler *et al., Proteins, Stuct. Func. Genet,* 9:180-190 (1991), the entirety of which is herein

incorporated by reference), for which both Macintosh and Microsoft Windows versions are available. MACAW uses a graphical interface, provides a choice of several alignment algorithms, and is available by anonymous ftp at: ncbi.nlm.nih.gov (directory/pub/macaw).

At page 48, lines 11 to 17:

A PCR probe is a nucleic acid molecule capable of initiating a polymerase activity while in a double-stranded structure with another nucleic acid. Various methods for determining the structure of PCR probes and PCR techniques exist in the art. Computer generated searches using programs such as Primer3 [(www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi)] (available on the World Wide Web at genome.wi.mit.edu/cgi-bin/primer/primer3.cgi), STSPipeline [(www-genome.wi.mit.edu/cgi-bin/www-STS_Pipleine)] (available on the World Wide Web at genome.wi.mit.edu/cgi-bin/www-STS_Pipleine) or GeneUp (Pesole *et al., BioTechniques 25*:112-123 (1998) the entirety of which is herein incorporated by reference), for example, can be used to identify potential PCR primers.

Marked-up Version of Amended Claims

1. (Amended) A substantially purified nucleic acid molecule that encodes a maize or a soybean adenine phosphoribosyl transferase[enzyme] or fragment thereof, wherein said nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 5 [maize or soybean enzyme is selected from the group consisting of:

(a) adenine phosphoribosyl transferase

(b) β glucosidase, and

(c) isopentyltransferase].